Human Subjects Timeline

Timeline of Laws Related to the Protection of Human Subjects

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In the past, the role of human research subject has been fraught with danger and suffering. The ancient Hippocratic Oath specified a duty from a physician to avoid harming the patient, but that oath, highly honored today, was not even subscribed to by a majority of doctors at the time. Advances in protection for human subjects have often come in response to particular abuses or scandals. The German atrocities of World War II, some of which were committed in the name of science, led to the Nuremberg Code of international ethics, which in part spelled out the requirement that any human subject must give informed consent to the research undertaken. The disaster of thalidomide in Europe and Canada was largely averted in the United States, but thousands of patients had taken doses without being informed of the drug's experimental nature. The brush with thalidomide helped the U.S. pass the 1962 Kefauver-Harris amendments, which strengthened federal oversight of drug testing and included a requirement for informed consent. A 1966 study of abuses, written by Dr. Henry K. Beecher, helped inform government policies adopted in that year. Likewise, the discovery in the 1970s that unwitting subjects had been allowed to suffer syphilis in the 1930s Tuskegee Experiment preceded a call for tighter regulation of federally-funded human research.

Between these unfortunate incidents, groups of regulators and researchers have worked to refine the protections provided to human subjects. By the 1990s, federal policy was made consistent across multiple agencies, and a series of ethical organizations and government commissions have continued to contribute to the literature of human subject research. A timeline of significant legislation, regulations and other developments appears below.

ANTIQUITY | 1938 | 1947 | 1949 | 1953 | 1953 | 1962 | 1963 | 1964 | 1966 | 1974 | 1978 | 1979 | 1980-1983 | 1981 | 1983 | 1991 | 1995 | 1995-2001 | 1996 | 2000 | 2001 | 2002 | 2012

ANTIQUITY

Milestone:
Hippocratic Oath
[See text / Download PDF - 8KB]
[Compare the current principles of ethics of the American Medical Association]
[Compare a modernized version of the Oath]

Status:
Code of professional ethics

Description:
Physician has an ethical responsibility to the patient as well as to the medical tradition.

top of page

1938

Milestone:
Food and Drug Act
[See web page for current Federal Food, Drug, and Cosmetic Act]

Status:
U.S. Law

Description:
Requires that drugs be shown to be safe before marketing. This leads to the need for human trials.

top of page

1947

Milestone:
Nuremberg Code
[See text / Download PDF - 4KB]

Status:
International code of ethics

Description:
Informed consent required for experiments.
Experiments must be scientifically necessary and conducted by qualified personnel.
Human trials should be preceded by animal studies and surveys of a disease's natural history.
Benefit to science must be weighed against risks and suffering of experimental subjects.

top of page

1949

Milestone:
International Code of Medical Ethics of the World Medical Assembly, including the Declaration of Geneva
[See text / Download PDF - 8KB]

Status:
International code of professional ethics

Description:
A physician shall always bear in mind the obligation of preserving human life.
The health of the patient shall be the physician's first consideration.
A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient.

top of page

1953

Milestone:
NIH Clinical Center policy
Download PDF of human subject policy - 564KB]

Status:
Agency policy

Description:
Ethical responsibility for medical experiments lies with the study's principal investigators.

top of page

1953

Milestone:
NIH Medical Board Document No.1
[Download NIH Clinical Center human subject policy- 249KB]

Status:
Agency policy

Description:
Ethical responsibility for developing policies governing standards of medical care in the Clinical Center.

top of page

1962

Milestone:
Kefauver-Harris amendments to the 1938 Food, Drug, and Cosmetic (FD&C) Act
Public Law 87-781; 76 Stat. 788-89

Status:
First U.S. law requiring informed consent

Description:
FDA empowered to ban drug experiments in humans pending animal trials for safety.

top of page

1963

Milestone:
FDA regulations
[21 CFR 130.3, later incorporated in 45 CFR 46 (see below)]

Status:
U.S. Regulations

Description:
Clinical investigators required to certify informed consent as required by the Kefauver-Harris amendments.

top of page

1964

Milestone:
Helsinki Declaration signed by U.S. (revised in 1975, 1983, 1989)
[See text / Download PDF - 8KB]

Status:
International ethical guidelines

Description:
Clinical research should be based on animal and laboratory experiments.
Clinical research should be conducted and supervised only by qualified medical workers.
Clinical research should be preceded by a careful assessment of risks and benefits to the patient.
Human beings should be fully informed and must freely consent to the research.
Responsibility for the human subject must always rest with a medically qualified person, and never with the subject.
Results of experiments that do not comply with ethical guidelines should not be accepted for publication.
Special care must be taken with informed consent of minors.
Also mentions consideration of the welfare of animal subjects and the environment.

top of page

1966

Milestone:
U.S. Surgeon General policy statement
["Clinical research and investigation involving human beings," Surgeon General, Public Health Service to the Heads of the Institutions Conducting Research with Public Health Service Grants]
[Download U.S. Surgeon General Policy PDF - 489KB]

Status:
U.S. policy

Description:
All human subject research requires independent prior review. Origin of Institutional Review Boards (IRBs).

Milestone:
FDA regulations
[21 CFR 130.37, later incorporated in 45 CFR 46 (see below)]

Status:
U.S. Regulations

Description:
Specific requirements of informed consent defined.

top of page

1974

Milestone:
National Research Act
[Title II, Public Law 93-348]
[Download PDF - 380KB]

Status:
U.S. Law

Description:
Regulations to be codified.
All research funded by DHEW to be reviewed by IRBs.

Milestone:
Regulations for the Protection of Human Subjects of Biomedical and Behavioral Research
[45 CFR 46]
[See Text / Download PDF - 116KB]

Status:
U.S. Regulations

Description:
IRB procedures established.

Milestone:
45 CFR 46 Subpart B
[see current 45 CFR 46 above]

Status:
U.S. Regulations

Description:
Special protections for pregnant women and fetuses.

top of page

1978

Milestone:
45 CFR 46 Subpart C
[see current 45 CFR 46 above]

Status:
U.S. Regulations

Description:
Special protections for prisoners.

top of page

1979

Milestone:
Belmont Report (Report on Ethical Principles and Guidelines for the Protection of Human Subjects of Research), issued by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (National Commission)
[See text / Download PDF - 32KB]

Status:
U.S. ethical guidelines

Description:
Principal of Respect: recognizes the autonomy of humans and requires clear informed consent.
Principal of Beneficence: Research must be shown to be beneficial and reflect the Hippocratic idea of do no harm.
Principle of Justice: The benefits to some must be balanced against the risks to subjects.

top of page

1980-1983

Milestone:
President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research (President's Commission)

Status:
Recommendations became basis of 10 CFR 745 ("Common Rule", below)

Description:
Recommended that all federal agencies adopt the human subject regulations of the Department of Health and Human Services (DHHS, formerly DHEW).

top of page

1981

Milestone:
FDA regulations revised.
Informed consent [21 CFR 50]
[See text / Download PDF - 72KB]

IRBs [21 CFR 56]
[See text / Download PDF - 72KB]

Status:
U.S. Regulations

Description:
Revised to correspond to DHHS regulations.

top of page

1983

Milestone:
45 CFR 46 Subpart D
[see current 45 CFR 46 above]

Status:
U.S. Regulations

Description:
Special protections for children.

top of page

1991

Milestone:
Common Federal Policy for the Protection of Human Subjects ("Common Rule")
[10 CFR 745]
[See text / Download PDF - 84KB]

Status:
U.S. Regulations

Description:
Sixteen agencies adopt the regulations of 45 CFR 46 subpart A.
Subparts B, C, D adopted by many agencies.

top of page

1995

Milestone:
Final report of Advisory Committee on Human Radiation Experiments (created in 1994)
[Report at Archive-It]

Status:
Report

Description:
Further means required to ensure highest ethical standards.
Special care to be taken where research must be kept secret.

top of page

1995-2001

Milestone:
National Bioethics Advisory Commission (NBAC)
[Download list of publications PDF - 192KB]

Status:
Series of ethical and policy reports

top of page

1996

Milestone:
FDA regulations revised.
[21 CFR 50.24]
[See text / Download PDF - 52KB]

Status:
U.S. Regulations

Description:
Allows exception from informed consent requirements for research studies involving emergency research.

Milestone:
International Conference on Harmonisation, Guideline E6: Good Clinical Practice, Consolidated Guideline
[Download PDF - 264KB]

Status:
International guidelines

Description:
Good clinical practice as an inernational standard that provides public assurance that trial subjects are protected. U.S., E.U, Japan are all signatories.

top of page

2000

Milestone:
World Health Organization Operational guidelines for ethics committees that review biomedical research
[View webpage / Download PDF - 76KB]

Status:
International guidelines

Description:
Intended to facilitate and support ethical review in all countries around the world. Suggests role, constituents and requirements for ethics committees.

top of page

2001

Milestone:
Best Pharmaceuticals for Children Act
Download PDF - 76KB

Status:
U.S. Law

Description:
Provides six-month patent extension for manufacturers who conduct voluntary pediatric trials.

top of page

2002

Milestone:
Suspension of rule requiring pediatric studies of medicines for children.
[View *AAP News* Vol. 20 No. 5 May 2002, p. 200 © 2002 American Academy of Pediatrics article]

Status:
FDA rule

Description:
Two-year suspension of 1997 rule. Safety concerns considered addressed by incentive under Best Pharmaceutical for Children Act, above.

top of page

2012

Milestone:
FDA has prepared this guidance in accordance with section 212 of the Small Business Regulatory Enforcement Fairness Act. It is intended to help small businesses better understand the new informed consent requirements set forth in 21 CFR § 50.25(c).
View Guidance for Sponsors, Investigators, and Institutional Review Boards

Status:
FDA rule

Description:
For applicable clinical trials initiated on or after March 7, 2012, informed consent documents must be in compliance with the new requirement in 21 CFR § 50.25(c) and include a specific statement that refers to the trial's description on www.ClinicalTrials.gov.

top of page